UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

14/OCT/2004

MEMORANDUM

Subject:	Name of Pesticide Product:	F4113 EW Herbicide
	EPA Reg. No. /File Symbol:	279-GEOG
	DP Barcode:	D308883
	Decision No:	348285
	PC Codes:	128712, 103601

From: Eugenia McAndrew, Biologist
Technical Review Branch
Registration Division (7505C)

To: Vickie Walters, RM Team 25
Herbicide Branch
Registration Division (7505C)

Applicant: FMC Corporation
1735 Market Street
Philadelphia, PA 19103

FORMULATION FROM LABEL:

	Active Ingredient(s):	% by wt.
128712	Carfentrazone-ethyl	0.99
103601	Glyphosate IPA	49.71
	Inert Ingredient(s):	49.30
	Total:	100.0%

ACTION REQUESTED: RM requests review of acute toxicity data for F4113 EW Herbicide, EPA File Symbol 279-GEOG.

BACKGROUND: FMC Corporation has submitted a six pack of acute toxicity studies to support the registration of F4113 EW Herbicide, EPA File Symbol 279-GEOG. The studies were conducted at Charles River Laboratories, Inc., Discovery and Development Services, Spencerville, Ohio with assigned MRID numbers 46351502-02 to -07.

RECOMMENDATIONS: The six studies have been reviewed and are classified as acceptable.

The acute toxicity profile for F4113 EW Herbicide, EPA File Symbol 279-GEOG, is as follows:

acute oral toxicity	IV	Acceptable	MRID 46351502
acute dermal toxicity	IV	Acceptable	MRID 46351503
acute inhalation toxicity	IV	Acceptable	MRID 46351504
primary eye irritation	III	Acceptable	MRID 46351505
primary skin irritation	IV	Acceptable	MRID 46351506
dermal sensitization	Negative	Acceptable	MRID 46351507

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System.

PRODUCT ID #: 000279-03293

PRODUCT NAME: F4113 EW Herbicide

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: CAUTION

Causes moderate eye irritation. Avoid contact with eyes or clothing. Wear: Long-sleeved shirt and long pants, socks, shoes, and gloves.

First Aid:

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

User Safety Recommendations:

Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco.

Reviewer: Eugenia McAndrew October 14, 2004
Risk Manager: 25

STUDY TYPE: Acute Oral Toxicity - S-D Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid)

CITATION: Rodabaugh, D. An Acute Oral Toxicity Study in Rats with Carfentrazone-ethyl + Glyphosate IPA EW (Up/Down Study Design). Charles River Laboratories, Inc. Laboratory Report Number KZH00007. August 25, 2004. MRID 46351502. Unpublished.

SPONSOR: FMC Corporation, P.O. Box 8, Route 1 North & Plainsboro Rd., Princeton, NJ 08543

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46351502), three female Hsd: Sprague-Dawley SD young adult rats (Age:11-12 weeks; Source: Harlan Sprague Dawley, Inc., Indianapolis, IN; 208-224 g) were given a single oral dose of Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid) using the Up and Down Procedure. A limit dose of 2000 mg/kg of the test substance was administered to one healthy female rat by oral gavage. Due to the absence of mortality in this animal, the dose level was increased to 5000 mg/kg and dosed in one animal. Since there was no mortality, two additional female rats were tested at the same level to complete the limit test. Animals were then observed for 14 days.

Oral LD_{50} Females => 5000 mg/kg bw

All animals survived at the 2000 and 5000 mg/kg dose levels. Clinical signs noted at both doses included few feces and dark material around the nose. In addition, congested breathing, urine stain and rough haircoat were noted at 5000 mg/kg. The animals recovered from these symptoms by day 4. All animals gained weight. Gross necropsy revealed no gross abnormalities.

Toxicity based on the lack of deaths at the limit dose of 5000 mg/kg. EPA Toxicity Category IV.

This acute oral study is classified as acceptable. It does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 425) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Individual animals were dosed as follows:

Limit Test

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short Term Outcome	14 Day Outcome
1	A9410	2000	S	S

Dosing Sequence	Animal No.	Dose level (mg/kg)	Short Term Outcome	14 Day Outcome
1	A9411	5000	S	S
2	A9453	5000	S	S
3	A9407	5000	S	S

S = survival D = death

A. Mortality - as noted in table

B. Clinical observations - All animals survived at the 2000 and 5000 mg/kg dose levels. Clinical signs noted at both doses included few feces and dark material around the nose. In addition, congested breathing, urine stain and rough haircoat were noted at 5000 mg/kg. The animals recovered from these symptoms by day 4. All animals gained weight.

C. Gross Necropsy - No gross abnormalities were observed.

D. Reviewer's Conclusions: Agree with the study author

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Wednesday, October 13, 2004, 2:36:42 PM
Data file name: F4112.dat
Last modified: 10/13/2004 2:36:38 PM

Test/Substance: Enter test description.
Test type: Main Test
Limit dose (mg/kg): 5000
Assumed LD50 (mg/kg): Default

Assumed sigma (mg/kg): 0.5

Recommended dose progression: 5000, 1750, 550, 175, 55, 17.5, 5.5, 1.75

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	A9410	2000	O	O
2	A9411	5000	O	O
3	A9453	5000	O	O
4	A9407	5000	O	O

(X = Died, O = Survived)

Dose Recommendation: The main test is complete.

WARNING:
Please review the data for accuracy.
Starting the Main Test above the likely LD50 will induce bias toward the starting dose. See OECD Guideline 425.

Stopping criteria met: 3 at Limit Dose.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
2000	1	0	1
5000	3	0	3
All Doses	4	0	4

Statistical Estimate based on long term outcomes:

The LD50 is greater than 5000 mg/kg.

Reviewer: Eugenia McAndrew October 14, 2004
Risk Manager: 25

STUDY TYPE: Acute Dermal Toxicity - S-D Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid)

CITATION: Rodabaugh, D. An Acute Dermal Toxicity Study in Rats with Carfentrazone-ethyl + Glyphosate IPA EW. Charles River Laboratories, Inc. Laboratory Report Number KZH00008. August 25, 2004. MRID 46351503. Unpublished.

SPONSOR: FMC Corporation, P.O. Box 8, Route 1 North & Plainsboro Rd., Princeton, NJ 08543

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 46351503), 5/sex of Hsd: Sprague-Dawley SD adult rats (Age:11-12 weeks; Source: Harlan Sprague Dawley, Inc., Indianapolis, IN; 313-338 g males and 203-214 g females) were dermally exposed to Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid). Five thousand mg/kg of the test substance was spread evenly over an area of approximately 10% of body surface. The test sites were covered with a porous gauze dressing (occlusive binding). The dressings were removed after a 24 hour period. Animals were then observed for 14 days.

Dermal LD_{50} Males => 5000 mg/kg bw
Dermal LD_{50} Females => 5000 mg/kg bw
Dermal LD_{50} Combined => 5000 mg/kg bw

All animals survived. Clinical signs noted included transient incidences of dark material around the facial area and urine stain. Dermal irritation was noted at the site of test material application. One female lost weight during days 7 to 14 but all animals exceeded initial body weights by study termination. No significant gross abnormalities were observed for any of the animals necropsied at the end of the study.

Toxicity based on the lack of deaths at the limit dose. EPA Toxicity Category IV.

This acute dermal study is classified acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Dosage (mg/kg bw)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

A. Mortality - as noted in table

B. Clinical observations - All animals survived. Clinical signs noted included transient incidences of dark material around the facial area and urine stain. Dermal irritation was noted at the site of test material application. One female lost weight during days 7 to 14 but all animals exceeded initial body weights by study termination.

C. Gross Necropsy - No significant gross abnormalities were observed for any of the animals necropsied at the end of the study.

D. Reviewer's Conclusions: Agree with the study author

Reviewer: Eugenia McAndrew October 14, 2004
Risk Manager: 25

STUDY TYPE: Acute Inhalation Toxicity -S-D rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid)

CITATION: Rodabaugh, D. An Nose-only Acute Inhalation Toxicity Study in Rats with Carfentrazone-ethyl + Glyphosate IPA EW. Charles River Laboratories, Inc. Laboratory Report Number KZH00009. August 25, 2004. MRID 46351504. Unpublished.

SPONSOR: FMC Corporation, P.O. Box 8, Route 1 North & Plainsboro Rd., Princeton, NJ 08543

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 46351504), 5/sex of Hsd: Sprague-Dawley SD young adult rats (Age:12 weeks; Source: Harlan Sprague Dawley, Inc., Indianapolis, IN; 347-378 g males and 185-207 g females) were exposed nose only via the inhalation route to Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid) at a concentration of 2.50 mg/L for 4 hours. Animals were then observed for 14 days.

LC_{50} Males => 2.50 mg/L
LC_{50} Females => 2.50 mg/L
LC_{50} Combined => 2.50 mg/L

All animals survived. Clinical signs observed were dark material around the facial area and few feces. Slight body weight loss was noted for two females during days 0 to 7 but all animals exceeded initial body weights by the end of the study. No gross internal findings were observed at necropsy. The analytical chamber concentration was 2.50 mg/L and the mass median aerodynamic diameter was estimated to be 3.6 μm with a geometric standard deviation of 1.86.

Toxicity based lack of deaths at the limit dose. EPA Toxicity Category IV.

This acute inhalation study is classified as acceptable. It does satisfy the guideline requirement for an acute inhalation study (OPPTS 870.1300; OECD 403) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Nominal Concentration (mg/L)	Analytical Concentration (mg/L)	MMAD µm	GSD µm	Mortality/Number Tested		
				Males	Females	Combined
163.81	2.50	3.6	1.86	0/5	0/5	0/10

Test Atmosphere / Chamber Description:

Chamber Volume:	**10 L**
Airflow:	**67 LPM**
Temperature:	**75-76°F**
Relative Humidity:	**51-5%**
Time to Equilibrium:	**2 min.**

A. **Mortality** - as noted in table

B. Clinical observations - All animals survived. Clinical signs observed were dark material around the facial area and few feces. Slight body weight loss was noted for two females during days 0 to 7 but all animals exceeded initial body weights by the end of the study. The analytical chamber concentration was 2.50 mg/L and the mass median aerodynamic diameter was estimated to be 3.6 µm with a geometric standard deviation of 1.86.

C. Gross Necropsy - No gross internal findings were observed.

D. Reviewer's Conclusions: Agree with the study author

Reviewer: Eugenia McAndrew October 14, 2004
Risk Manager: 25

STUDY TYPE: Primary Eye Irritation - NW Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid)

CITATION: Rodabaugh, D. A Primary Eye Irritation Study in Rabbits with Carfentrazone-ethyl + Glyphosate IPA EW. Charles River Laboratories, Inc. Laboratory Report Number KZH00010. August 25, 2004. MRID 46351505. Unpublished.

SPONSOR: FMC Corporation, P.O. Box 8, Route 1 North & Plainsboro Rd., Princeton, NJ 08543

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 46351505), 0.1 mL of Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid) was instilled into the conjunctival sac of the right eye of three adult New Zealand White male rabbits (Source: Myrtle's Rabbitry, Thompson Station, TN). The left eye served as the control. Animals were then observed at 1, 24, 48, 72 hours and at 7 and 10 days post-instillation. Irritation was scored by the method of Draize.

All three eyes exhibited conjunctivitis and iritis at the one hour observation and 2/3 eyes showed corneal opacity. By 72 hours, corneal opacity was still observed in one eye. The irritation decreased with time. No positive scores were noted on day 7.

In this study, formulation is moderately irritating. EPA Toxicity Category III.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION:

Observations	Number "positive"/number tested					
	Hours				Days	
	1	24	48	72	7	10
Corneal Opacity	2/3	3/3	2/3	1/3	0/3	0/3
Iritis	3/3	1/3	1/3	0/3	0/3	0/3
Conjunctivae:						
Redness	3/3	3/3	1/3	0/3	0/3	0/3
Chemosis	3/3	3/3	1/3	0/3	0/3	0/3
Discharge	3/3	0/3	0/3	0/3	0/3	0/3

*Score of 2 or more required to be considered "positive."

A. Observations - All three eyes exhibited conjunctivitis and iritis at the one hour observation and 2/3 eyes showed corneal opacity. By 72 hours, corneal opacity was still observed in one eye. The irritation decreased with time. No positive scores were noted on day 7.

B. Reviewer's Conclusions: Agree with study author

Reviewer: Eugenia McAndrew October 14, 2004
Risk Manager: 25

STUDY TYPE: Primary Dermal Irritation - NW Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid)

CITATION: Rodabaugh, D. A Primary Skin Irritation Study in Rabbits with Carfentrazone-ethyl + Glyphosate IPA EW. Charles River Laboratories, Inc. Laboratory Report Number KZH00011. August 25, 2004. MRID 46351506. Unpublished.

SPONSOR: FMC Corporation, P.O. Box 8, Route 1 North & Plainsboro Rd., Princeton, NJ 08543

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 46351506), three adult New Zealand White male rabbits (Source: Myrtle's Rabbitry, Thompson Station, TN) were dermally exposed to 0.5 mL of Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid). The test substance was applied to a 1 inch by 1 inch dose site on the dorsal area of each animal. Test sites were covered with a gauze pad which was held in place by tape. An elastic wrap (semi-occlusive) was placed over the trunk for a period of 4 hours. After the four-hour exposure, the binding materials were removed. Animals were then observed at 1, 24, 48 and 72 hours and up to 7 days after pad removal. Irritation was scored by the method of Draize.

In this study, formulation is a slight irritant. EPA Toxicity Category IV.

Primary Dermal Irritation Index (PDII) = 1.58 One hour after pad removal, very slight erythema was noted at all three test sites and very slight edema at one site. At 72 hours, very slight to well defined erythema was present at all three sites. All sites were free of irritation by day 7.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

A. Observations - One hour after pad removal, very slight erythema was noted at all three test sites and very slight edema at one site. At 72 hours, very slight to well defined erythema was present at all three sites. All sites were free of irritation by day 7.

B. Results - PDII - 1.58

C. Reviewer's Conclusions - Agree with study author

Reviewer: Eugenia McAndrew
Risk Manager: 25 October 14, 2004

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406

TEST MATERIAL: Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid)

CITATION: Rodabaugh, D. A Dermal Sensitization Study in Guinea Pigs with Carfentrazone-ethyl + Glyphosate IPA EW (Modified Buehler Design). Charles River Laboratories, Inc. Laboratory Report Number KZH00012. August 25, 2004. MRID 46351507. Unpublished.

SPONSOR: FMC Corporation, P.O. Box 8, Route 1 North & Plainsboro Rd., Princeton, NJ 08543

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46351507) with Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid), 30 young adult Hartley-derived albino guinea pigs (Source: Hilltop Lab Animals Scottdale, PA; Age: 7-8 weeks; 342-427 g males and 330-416 g females) were tested using the Modified Buehler study design. The procedures were validated using alpha-Hexylcinnamaldehyde (HCA) as the positive control substance.

Once each week for three weeks, 0.3 mL of undiluted test substance was applied to the left side of each animal for a 6-hour exposure period for a total of three exposures. Twenty-seven days after the first induction dose, 0.3 mL of undiluted test substance (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Ten naive control guinea pigs were also treated with the undiluted test substance at challenge only. Readings were made 24 and 48 hours after each induction application and after the challenge application.

In this study, the formulation is not a dermal sensitizer.

There were no dermal reactions in either the test or naive control groups at induction or challenge resulting scores of 0.0. The results of the HCA positive control study were appropriate to validate test procedures.

This study is classified as acceptable. It does satisfy the guideline requirement for a dermal sensitization study (OPPTS 870.2600; OECD 406) in the Guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. PROCEDURE

A. Induction - Once each week for three weeks, 0.3 mL of undiluted test substance was applied to the left side of each animal for a 6-hour exposure period for a total of three exposures. Readings were made 24 and 48 hours after each induction application.

B. Challenge - Twenty-seven days after the first induction dose, 0.3 mL of undiluted test substance (the highest non-irritating concentration) was applied to a naive site on each test animal for a 6-hour challenge exposure. Readings were made 24 and 48 hours after the challenge application.

C. Naive Controls - Ten naive control guinea pigs were also treated with the undiluted test substance at challenge only.

II. RESULTS and DISCUSSION:

A. Reactions and duration - There were no dermal reactions in either the test or naive control groups at induction or challenge resulting scores of 0.0. The results of the HCA positive control study were appropriate to validate test procedures.

B. Positive control - Results were appropriate to validate test procedures

C. Reviewer's Conclusions: Agree with study author

ACUTE TOX ONE-LINERS

1. DP BARCODE: D308883
2. PC CODES: 128712, 103601
3. CURRENT DATE: 14/OCT/2004
4. TEST MATERIAL: Carfentrazone-ethyl + Glyphosate IPA EW (Lot # PL04-0323; 0.95% Carfentrazone-ethyl and 50.8% Glyphosate IPA; off white liquid)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Charles River Laboratories, Inc. KZH00007/8-25-04	46351502	LD_{50} females > 5000 mg/kg	IV	A
Acute dermal toxicity/rat Charles River Laboratories, Inc. KZH00008/8-25-04	46351503	LD_{50} > 5000 mg/kg (males, females combined)	IV	A
Acute inhalation toxicity/rat Charles River Laboratories, Inc. KZH00009/8-25-04	46351504	LC_{50} > 2.50 mg/L (males females combined)	IV	A
Primary eye irritation/rabbit Charles River Laboratories, Inc. KZH00010/8-25-04	46351505	Corneal opacity, iritis and conjunctivitis in 3/3 eyes. No positive scores on day 7.	III	A
Primary dermal irritation/rabbit Charles River Laboratories, Inc. KZH00011/8-25-04	46351506	PDII = 1.58 Slight irritation at 72 hours	IV	A
Dermal sensitization/guinea pig Charles River Laboratories, Inc. KZH00012/8-25-04	46351507	Not a sensitizer	–	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived**